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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/888,824 | 06/25/2001 | Eric Perrier | 11123.24US01 | 9749 |

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| EXAMINER |
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HANLEY, SUSAN MARIE

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| ART UNIT | PAPER NUMBER |
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1651

DATE MAILED: 12/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

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|-----------------|----------------|
| Application No. | PERRIER ET AL. |
| 09/888,824 | |
| Examiner | Art Unit |
| Susan Hanley | 1651 |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 13 September 2004.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 69-94 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 69-94 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

| | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date <u>8/31/04</u> . | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Objections

Claim 69 is objected to because of the following informalities: The first line of the claim recites "A screening method comprising screening a compound...". The repetition of the word "screening" is redundant. It is suggested that the phrase be changed to "A screening method comprising testing a compound...". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 86-90 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for screening the extracts, as a whole, disclosed by the instant specification to inhibit LPL in order to identify at least one compound having slimming activity, does not reasonably provide enablement for screening the individual, isolated compounds in each disclosed extract to inhibit LPL in order to identify at least one compound having slimming activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims are given broadest reasonable interpretation and include all of the limitations of the independent claims. The independent claims are drawn to a method for screening at least a compound which is potentially active in the field of lipolysis. The phrase "at least a compound" encompasses an individual, isolated compound as well as mixtures of compounds. Claims 86-90 are drawn to screening

the extracts for at least a compound that inhibit LPL. In light of the independent claims from which claims 86-90 depend, the scope of these claims includes the extracts as a mixture as well as each isolated compound that makes up the extract. The specification is enabled for extracts as a whole of all the compounds that are in said extract, but the specification lacks disclosure that would enable the skilled artisan to isolate and analyze each extract to determine its exact chemical make up for the purpose of testing each compound in the extract by the claimed screening method. Isolation of natural products is unpredictable. For example, it took years of experimentation by many skilled researchers to isolate taxol. Therefore, natural products isolation and identification is unpredictable and the limited showing by the specification for screening extracts as whole mixtures for LPL inhibition is not sufficient to enable a claim drawn to screening the individual, isolated compounds comprising the disclosed extracts. Thus, the skilled artisan would have to engage in undue experimentation to practice the invention with the individual, isolated compounds that comprise each extract. The exception is St. John's wort because it has been analyzed to determine the active components. Thus, claims 86-90 are not commensurate in scope with the enabling disclosure.

Claims 87-89 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for screening a potentially active substance of an extract of the liana, *Uncaria tomentosa*, for the claimed method, does not reasonably provide enablement for screening all possible liana for the claimed method. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claims 87-89 are drawn in part to a method for screening a potentially active substance of an extract of the liana for identifying an LPL inhibitor and a slimming agent. The specification discloses one specie of liana, *Uncaria tomentosa*, as a potentially active substance for the claimed assay. However, there is no disclosure related to using any possible extract of any possible liana plant as a potentially active

substance. Moreover, the specification does not convincingly demonstrate how the skilled artisan would identify other suitable species of liana that would be potentially active substances for the claim assay.

Liana is not a plant specie. It is a common name that includes any of "various high-climbing, usually woody vines common in the tropics" (Webster's Dictionary, p. 689). According to *Encyclopedia Americana* web site, liana is a common name for numerous plants. For example, *Annonaceae* is a liana family that includes some 80 genera and about 850 species that can be found in India, Java, Africa and tropical America.

The limited showing of one specie of liana is not sufficient to enable a claim drawn to any possible liana because the art of botany is too unpredictable. One cannot assume that the ability of one particular type of liana to perform a special process ensures that all possible liana plants will have the same capability. Given the limited disclosure to one type of liana, *Uncaria tomentosa*, it would require undue experimentation for one of ordinary skill in the art to find and determine which species of liana are capable of being potentially active substances for the claimed assay. Thus, claims 87-89 are not commensurate in scope with the enabling disclosure.

Claims 69-94 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 69 and 92-94 are rejected because the "comprising a test of the capacity of the screened compound to inhibit LPL" is confusing. It is unclear how the compound can already be screened before it undergoes the screening process which is testing its ability to inhibit LPL.

Claims 69 and 92-94 are rejected because the phrase the "field of lipolysis" is vague and indefinite. Lipolysis is a reaction that splits complex lipids into smaller lipids. It is unclear how a reaction is a "field." Does "field mean the study of the enzymes that carry out a such a reaction, the study of non-enzymatic reactions that carry out such a reaction, the study of how lipolysis relates to some thing or process, or does it have some other meaning? The metes and bounds of the phrase are undefined.

Claim 69 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: The directions to carry out each step of the assay and how one correlates the effect of the test compound with the object of each claim: slimming activity in claim 69, diminishing or slowing down the fatty deposits in claim 92, increasing blood circulation in claim 93 and diminishing the ugly "orange peel" appearance in claim 94.

Claim 70 is rejected because the parenthetical expression "(potentially active substance)" is vague and indefinite. It is unclear if it modifies the phrase that precedes it or if it is intended to be a subset of said preceding phrase or that it means something else.

Claim 70-73 and 83 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: Determining how one correlates the effect of the test compound on slimming activity.

Claim 73 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: There is no step that compares the modulation of the known LPL inhibitor to that of the test compound. The claim also lacks a step that correlates said modulation comparison between the known LPL inhibitor and the test compound with slimming activity.

Claim 88 is rejected because "said extract" lacks antecedent basis in claim 69.

Claim 92 is rejected because the phrase "diminishing or slowing down the fatty deposits" is unclear. "Slowing down" implies that something is moving. It is suggested that the phrase be changed to "decreasing fatty deposits" or "decreasing the rate of fatty deposits."

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 69 and 92 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Cook et al. (US 5,244,798).

Using Webster's Dictionary, one can ascertain the broadest reasonable interpretation of the term "slimming" which is defined as: to make or become thin or slim (p. 1094). Cook et al. teach that the aim of their invention is to discover an effective way to control the body fat and/or body weight of an animal (col. 1, lines 37-40) and they recognize that the modulation of adipocyte LPL is essential to fat accumulation (col. 1, lines 58-59) which meets the "slimming" limitation, "for diminishing or slowing down the fatty deposits" recited in claims 92 because inhibiting LPL will result in less deposition of fat. Cook et al. meet the claim limitation for "slimming" because controlling body fat and/or body weight is synonymous with slimming activity. Cook et al. employ a screen using inhibition of LPL by candidate compounds and correlate the inhibition as an indication of the compound's ability to potentially control the body fat and/or body weight of an animal.

Claim 69 and 88 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Halvorsen et al. (US 2001/0041708).

Halvorsen et al. disclose a method of screening for lipolysis inhibitors for the purpose of identifying compounds that reduce lipolytic action thereby improving the aesthetic appearance of the skin. Halvorsen et al. teach that cellulite or "orange peel skin" is an example of excessive fat deposition (sections [0003]-[0005]). The assay for testing lipolysis comprises exposing cultured human adipocytes to the test compounds and measuring the resulting lipolytic activity ([sections [0077]-[0078]). LPL is inherently present in adipocytes. Halvorsen teaches that vegetable extract can be tested for slimming activity ([section 0008]).

Claim 93 is rejected under 35 U.S.C. 102(b) as being clearly anticipated by Carroll et al. (Lipids, 1982, vol. 27, p.4).

Carroll et al. disclose testing the effect of the potential inhibitor, U-57,908, on the activity of LPL in cardiac myocytes (abstract). Carroll et al. teach that LPL is bound to the luminal surface of capillary endothelial cells and that the enzyme has a functional role in lipoprotein metabolism (p. 306, right column). U-57,908 inhibited LPL thereby inhibiting the hydrolysis of fatty acids of acylglycerol substrates. Microcirculation encompasses capillary blood vessels since they are small and responsible for circulation. Thus, the disclosure by Carroll et al. meets the claim because inhibition of lipids onto capillary endothelial blood vessels would prevent narrowing of the blood vessels thereby increasing microcirculation.

Claim Rejections - 35 USC § 103

Claims 70-86 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Cook et al. (US 5,855,917), Wagle et al. (US 6,326,396), Takahashi et al. (US 5,955,072), Takeda et al. (US 5,244,798), Vainio et al. (1982), Cheng et al. (1990), Carroll et al. (1992) and Bensadoun et al. (1974) in view of NEFA-C kit from Wako in view of NEFA-C Kit instructions and Kikuchi et al. (US 4,301,244).

Applicant argues that the prior art does not teach or suggest using lipolysis by LPL as a screening method for compounds that provide slimming activity, diminish or slow fatty deposits or improve the appearance of skin. Applicant asserts that the intentions of the references cited for the instant rejection are directed to other purposes. Applicant states that Cook et al. aim to provide inhibitors in the field of reduction of fat accumulation and cites Ex. 4 and only illustrates one type of inhibitor of LPL. Applicant argues that Takeda et al. is directed to disclosing a thermostable LPL and teaching a method for determination of triglycerides in body fluids. Vainio et al. is directed to the study of the inhibition of LPL by benzene boronic acid. Applicant states that Wagle relates to a method of reducing hyperlipidemia and hyperglycemia and that there is not suggestion from Wako (NEFA-C) kit or Kikuchi et al. to carry out the present assay for the newly claimed intended uses. Applicant points to the opinion from the German

Patent Office that the instantly claimed invention has been found to be novel and inventive over the prior art.

Applicant's arguments filed 8/31/04 have been fully considered but they are not persuasive.

The opinions and actions by the German Patent Office are respected but Applicant is reminded that patentability of the instant invention in the United States is based solely on U.S. patent laws.

Responding to Applicant's argument that none of the references teaches the use of an LPL assay to determine compounds suitable for slimming activity, it is noted the MPEP directs Examiner's to make the broadest reasonable interpretation of the claims, absent an explicit definition from the specification of the application being examined. Using Webster's Dictionary as a basis for the broadest reasonable interpretation, the definition of "slimming" is to make or become thin or slim (p. 1094). Cook et al. teach that the aim of their invention is to discover an effective way to control the body fat and/or body weight of an animal (col. 1, lines 37-40) and they recognize that the modulation of adipocyte LPL is essential to fat accumulation (col. 1, lines 58-59). Controlling body fat and/or body weight is synonymous with "slimming activity" because one way to control one's weight or body fat is to lose it. Example 3 clearly demonstrates that the invention of Cook et al. is drawn to weight loss because they consider the loss of body fat by pigs that had taken the disclosed LPL inhibitors to be successful. The observation that Cook et al. only examine one type of inhibitor is not relevant because the claims do not state a limitation regarding how many types of inhibitors must be examined. Even if such a limitation was present, it would still be obvious to employ the LPL assay disclosed by Cook et al. to determine other compounds suitable for fat and/or weight loss because Cook et al. recognizes that connection between inhibition of adipocyte LPL and control of body and/or fat content and the supporting references demonstrated that a number of compounds are capable of inhibiting LPL.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231

USPQ 375 (Fed. Cir. 1986). The supporting references for the instant rejection are employed to address technical aspects of the assay in the dependent claims. It is not necessary that each of these references be directed to "slimming cavity" because the main reference, Cook et al. has been shown to read directly on the intended use of the instant invention. LPL assays are well known in the art and the cited references teach technical aspects of the instant invention not directly taught by Cook et al. One of these technical aspects, which was discussed in the interview of 10/30/04, is the use of triolein as a substrate for the LPL assay. Takeda et al. clearly shows that triolein is a suitable substrate for LPL and therefore an obvious substrate choice to for any LPL assay.

Claims 69-88 and 91 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cook et al. (US 5,855,917), Wagle et al. (US 6,326,396), Takahashi et al. (US 5,955,072), Takeda et al. (US 5,244,798), Vainio et al. (1982), Cheng et al. (1990), Carroll et al. (1992) and Bensadoun et al. (1974) in view of NEFA-C kit from Wako in view of NEFA-C Kit instructions and Kikuchi et al. (US 4,301,244) as applied to claims 69-86 above, and further in view of Halvorsen et al. (US 2001/0041708).

The combined disclosures of Cook et al., Wagle et al., Takahashi et al., Takeda et al., Vainio et al. (1982), Cheng et al. (1990), Carroll et al. (1992), Bensadoun et al. (1974), the NEFA-C kit instructions and Kikuchi et al. (US 4,301,244) are disclosed *supra*.

The combined disclosures do not suggest that the potentially active substance is an extract of St. John's wort.

Halvorsen teaches that vegetable extracts such St. John's wort as can be tested for slimming activity ([section 0008]).

It would have been obvious to one of ordinary skill in the art that an extract of St. John's wort would have been a potentially active substance for the disclosed slimming assay because Halvorsen et al. teach that it is a slimming agent and suitable for testing. The ordinary artisan would have had a

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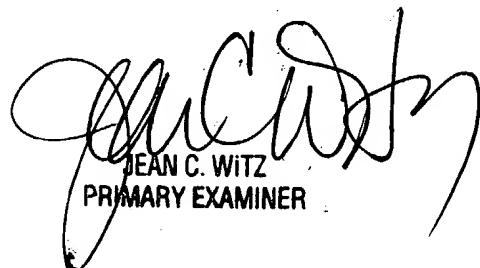
reasonable expectation of success that an extract of St. John's wort would have been a potentially active substance because its slimming activity was already known in the prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Hanley whose telephone number is 571-272-2508. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. *This is a new official FAX number.*

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Susan Hanley
Patent Examiner
AU 1651



JEAN C. WITZ
PRIMARY EXAMINER